



PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Derek van der Kooy et al.	Art Unit:	1636
Serial No.:	09/333,248	Examiner:	R. Yucel
Filed:	June 15, 1999	Customer No.:	21559
Title:	PHARMACEUTICALS CONTAINING RETINAL STEM CELLS		

Commissioner for Patents
Washington, DC 20231

SECOND DECLARATION OF DR. VINCENT TROPEPE UNDER 37 CFR §1.132
TRAVERSING GROUNDS OF REJECTION

Under 37 C.F.R. §1.132 and regarding the rejection of claims 5-8 under 35 U.S.C. § 112, first paragraph, for lack of enablement, I declare:

1. I am a named inventor of the subject matter claimed in United States Patent Application Serial No. 09/333,248 filed on June 15, 1999.
2. I received my Ph.D. in Developmental Biology in 2000 from the University of Toronto. I am currently a post-doctoral fellow at the Massachusetts Institute of Technology. I have authored over 9 peer-reviewed research publications in developmental biology and neuroscience.
3. I have read and understood the Office Action, dated July 16, 2002. This Declaration is presented to overcome the rejection of claims 5-8 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

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4. The methods of the invention have been used by researchers working under the direction of both myself and Dr. van der Kooy, also an inventor on the above-referenced application, to successfully and reliably demonstrate intraocular transplantation of retinal stem cells and retinal stem cell-derived cells, and to demonstrate that these cells have the potential for differentiating into mature retinal cells.

5. The transplantation methods employed to practice the presently claimed method were known to those skilled in the art of cellular transplantation at the time the application was filed or are provided by the instant specification. Examples of publications that demonstrate the knowledge and level of skill in the art at the time the application was filed are as follows:

1. Muller-Jensen et al., *Mod. Probl. Ophthalmol.* 15:228-234, 1975;
2. Whiteley et al., *Experimental Neurology* 140:100-104, 1996; and
3. He et al., *Graefes Arch. Clin. Exp. Ophthalmol.* 231:737-742, 1993.

6. The experiments described in paragraphs 5-9 of my previous Declaration filed April 11, 2002, were performed using a mouse model. This model is accepted by skilled artisans working in the field of retinal cell transplantation as predictive of transplantation success in humans. The skilled artisan would also conclude, based on pre- and post-filing art, that some or all retinal function can be restored by replenishing retinal cells that have been lost due to damage or disease, and that success in the mouse model would again be predictive of success for the restoration of function in humans.

7. The data described in paragraph 6 of my previous Declaration clearly demonstrate the successful intraocular transplantation of retinal stem cell-derived cells, and further, that these cells differentiate into retinal neurons, in particular, photoreceptors. In addition, the results of the experiments revealed no abnormal retinal development or adverse immune response.

8. Based on the results of the experiments provided in my previous Declaration, I concluded that this method would be useful for the treatment of diseases or disorders, or

abnormal physical states of the retina of the eye. Furthermore, I believe that it is reasonable to conclude that one skilled in the art would also reasonably draw this conclusion. This is evidenced by the following references:

1. He et al., Graefes Arch. Clin. Exp. Ophthalmol. 231:737-742, 1993;
2. Sauvé et al., Experimental Neurology 152:243-250, 1998; and
3. Whiteley et al., Experimental Neurology 140:100-104, 1996.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date:

1/16/03


Vincent Tropepe

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